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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,951	01/29/2002	Paul A. Moore	PF378P1D1	4875

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	6

DATE MAILED: 05/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,951	MOORE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

P riod f r R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19 and 21-183* is/are pending in the application.

4a) Of the above claim(s) *45-46,79,104-105 and 138* is/are withdrawn from consideration.

5)☒ Claim(s) *145-161,163-177 and 179-183* is/are allowed.

6)☒ Claim(s) *19,21-44,47-78,80-103,106-137 and 139-144, 162 and 178* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 19, 21-183 are pending.

2. Applicant's election with traverse of Group III, claim 19 (now claims 19, 21-44, 47-78, 80-103, 106-137 and 139-183) drawn to an antibody or fragment thereof that specifically binds to t-PALP filed on 3/19/03, is acknowledged.

Applicant's traversal is on the grounds that the restriction is improper unless the examiner can show that the search and examination of these groups would entail a "serious burden". Applicant argues that the searches for proteins, nucleic acids encoding such proteins, antibodies to such proteins, and methods of making and using the same commonly overlap. Further applicant argues that a reasonable number, normally ten sequences, will be examined in a single application. This is not found persuasive because Groups I-IV are classified in different Classes and are recognized divergent subject matter. Contrary to Applicant's assertions, each of the nucleic acids SEQ ID NO is distinct sequence and must be individually searched in the patent and non-patent literature; therefore, serious burden exists to examine more than one SEQ ID NO in a single application. Therefore a DNA encoding t-PALP protein, t-PALP protein, antibodies against t-PALP protein are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 45-46, 79, 104-105 and 138 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 19, 21-44, 47-78, 80-103, 106-137 and 139-183 are under examination as they read on an antibody or fragment thereof that specifically binds to t-PALP.

5. The U.S. Patent 6,372,473 cited on the PTO FORM 892 is issued from the parental application serial No. 09/411,977 and will not be supplied.

6. The specification on page 1 should be amended to reflect the status of parent application Nos. 09/411,977 and 09/084,491.

7. The specification is objected to because of the following: Figure 2 shows an alignment of t-PALP and human t-PA. SEQ ID NO:2 consisting of 263 amino acids is aligned with residues 191-516 of t-PA. On page 8, line 9, the t-PA sequence is referred to as SEQ ID NO:3. SEQ ID NO:3 has 372 amino acids. Residues 191-516 of t-PA on Figure 2 correspond to residues 1-326 of SEQ ID NO:3. Appropriate correction is required.

8. Claim 19 is objected to because it is dependent on a canceled claim 17 and should be written as an independent claim.

9. The declaration of biological deposit and the statement concerning ATCC Deposit No. 209023, filed 01/26/01 (Paper No. 12) and 10/5/01 (Paper No. 16), in parent application 09/411,977 are sufficient to satisfy the requirement for the deposit of biological materials under 35 U.S.C. § 112, first paragraph.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 41, 75, 100, 134 and 139-144 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The "the antibody or portion thereof" recited in claims 41, 75, 100 and 134 has no antecedent basis in base claims 23, 58, 82 and 117, respectively. Base claims 23, 58, 82 and 117 only recite an antibody or fragment thereof.

B. The "operably associated" recited in claim 139, line 3 is indefinite and ambiguous. It is unclear whether the polynucleotide is linked direct or indirect through covalent or non-covalent bond. For example, in a complex of A, B, and C, A can associate with C directly, or indirectly through B.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 34, 93, 127, 162 and 178 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "a luminescent label" claimed in claims 34(c), 93(c), 127(c), 162(c) and 178(c) and "a bioluminescent label" claimed in claims 34(d), 93(d), 127(d), 162(d) and 178(d) represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 3/19/03 points to the specification on pages 5(¶16), 6(¶17-18), 84(¶203), 113(¶307), for support for the newly added limitations "a luminescent label" and "a bioluminescent label" as claimed in claims 34, 93, 127, 162 and 178. Examiner noticed that page 113(¶307) discloses enzyme labels such as glucose oxidase and radioisotopes, however, the specification does not provide a clear support of "a luminescent label" and "a bioluminescent label". The instant claims now recite limitations which were not clearly disclosed in the specification and claims as originally filed.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 19, 21-44, 47-78, 80-103 and 106-137 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or antigen binding fragment thereof that specifically binds amino acids –20 to 242, 1 to 242, 4 to 63, 64 to 242, 1 to 10, 14 to 23, 50 to 60, 70 to 86, 98 to 107, 117 to 126, 134 to 146, 172 to 182, 185 to 194, 206 to 216 and 22 to 231 of SEQ ID NO: 2, does not reasonably provide enablement for any isolated antibody that binds specifically to any t-PALP polypeptide "comprising" an amino acid sequence at least 95% identical to amino acids –20 to 242, 1 to, 242, 4 to 63, 64 to 242 of SEQ ID NO:2 or as encoded by cDNA clone contained in the ATCC Deposit No. 209023 in canceled base 17, an isolated antibody or fragment thereof that specifically binds to a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2 in claims 21(e and f), 47 (e and f), 56 (e and f), 80(e and f), 106(e and f) and 115 (e and f). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There is insufficient guidance and direction as to make and use antibodies, wherein the antibodies or antigen binding fragments thereof binds "a polypeptide comprising any amino acid sequence at least 95% identical" to –20 to 242, 1 to, 242, 4 to 63, 64 to 242 of SEQ ID NO: 2 or as encoded by cDNA clone contained in the ATCC Deposit No. 209023 or a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2.

Claims 19, 21(e and f), 47 (e and f), 56 (e and f), 80(e and f), 106(e and f) and 115 (e and f) require antibody to bind to different polypeptides. However, the present specification fails to provide sufficient disclosure of amino acid portions that maintain the structural and functional properties of the tissue plasminogen activator-like protease set forth in SEQ ID NO:2, wherein the portions are comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2, or

a polypeptide at least 95% sequence identity to the amino acids –20 to 242, 1 to, 242, 4 to 63, 64 to 242 of SEQ ID NO:2 which include numerous changes and variation. The specification does not provide sufficient guidance as to which of the amino acids may be changed while t-PALP functional activity is retained. In addition, the term "comprising" in canceled base claim 17 is open-ended, it expand the "t-PALP polypeptide" of the amino acid sequence of SEQ ID NO: 2 to include additional non disclosed amino acids.

The one of the uses of the claimed polypeptide is to make antibody then any change in the polypeptide of SEQ ID NO: 4 would affect the binding specificity of the antibody. Colman *et al* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza *et al* in Journal of Protein Chemistry (11(5):433-444, 1992) teach that single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Futher, Lederman *et al* in Molecular Immunology (28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Additionally, Li *et al* in PNAS (77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

Because of this lack of guidance, an undue experimentation would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo *et al* in the Protein Folding problem and Tertiary Structure prediction, 1994, Merz *et al.*, (ed), Birkhauser, Boston, MA, pp.433 and 492-495), it would require an undue amount of experimentation for one of skill in the art to arrive at the claimed fragments having galectin activity; its immunogenic fragments or amino acid sequence having 90% sequence identity to the sequence of SEQ ID NO:1 encompassed by the claimed invention

The scope of the claimed antibodies that is specifically binds to SEQ ID NO:2 is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of amino acid sequences broadly encompassed by the claimed invention as recited in the canceled base claim 17, 21(e and f), 47 (e and f), 56 (e and f), 80(e and f), 106(e and f) and 115 (e and f). Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's or peptide's amino acid sequence and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

16. Claims 19, 21-44, 47-78, 80-103 and 106-137 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an antibody or antigen binding fragment thereof that specifically binds amino acids –20 to 242, 1 to 242, 4 to 63, 64 to 242, 1 to 10, 14 to 23, 50 to 60, 70 to 86, 98 to 107, 117 to 126, 134 to 146, 172 to 182, 185 to 194, 206 to 216 and 22 to 231 of SEQ ID NO: 2.

Applicant is not in possession of any isolated antibody that binds specifically to any t-PALP polypeptide "comprising" an amino acid sequence at least 95% identical to amino acids –20 to 242, 1 to, 242, 4 to 63, 64 to 242 of SEQ ID NO:2 or as encoded by cDNA clone contained in the ATCC Deposit No. 209023 in canceled base 17, an isolated antibody or fragment thereof that specifically binds to a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2 in claims 21(e and f), 47 (e and f), 56 (e and f), 80(e and f), 106(e and f) and 115 (e and f).

Applicant has disclosed only amino acid of SEQ ID NO: 2 and the specific fragments; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath

at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

17. Claims 145-161, 163-177 and 179-183 are allowed.

18. Claims 139-144 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, second paragraph, set forth in this Office action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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May 1, 2003

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